PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 4 : C12P 21/02, G01N 33/53 // C07K 15/18, C07H 21/04 C12N 15/00 (C12N 5:00 C12R 1:91)

A1

(11) International Publication Number: WO 89/ 02472

(43) International Publication Date: 23 March 1989 (23.03.89)

(21) International Application Number: PCT/AU88/00370

(22) International Filing Date: 21 September 1988 (21.09.88)

(31) Priority Application Numbers: PI 4493
PI 6787

(32) Priority Dates: 21 September 1987 (21.09.87)
16 February 1988 (16.02.88)

(33) Priority Country: AU

(71) Applicant *(for all designated States except US)*: AMRAD CORPORATION LIMITED [AU/AU]; 663 Victoria Street, Abbotsford, VIC 3067 (AU).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)* : SHANNON, Mary, Frances [IE/AU]; 8 the Crescent, Crafers, S.A. 5152 (AU). VADAS, Mathew, Alexander [AU/AU]; 8 Branch Road, Stirling, S.A. 5152 (AU).

(74) Agents: SLATTERY, John, Michael et al.; Davies & Collison, 1 Little Collins Street, Melbourne, VIC 3000 (AU).

(81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.

Published
With international search report.
With amended claims.

Date of publication of the amended claims:
20 April 1989 (20.04.89)

(54) Title: REGULATION OF EXPRESSION OF GM-CSF GENE

GENE	SEQUENCE
	-96 -75
hGM-CSF (5)	GGAGATTCCACAGTTCAGGTA
	-108 -88
mGM-CSF (15)	GGAGATTCCACAacTCAGGTA
hIL-3 (Yang et al, in press)	GGAGgTTCCAt-G-TCAGaTA
	-115 -97
hIL-3 (31)	GGAGgTTCCAt-G-TCAGaTA
	-198 -178
hIL-2 (32)	aGgGATTtCACctacatccat
	-208 -188
mIL-2 (33)	aGgGATTtCACctaaatccat
	-188 -168
hG-CSF (34)	aGAGATTCCACAaTTtcacaA
	-172 -172
mG-CSF (16)	aGAGATTCCcCgaTTtcacaA

(57) Abstract

A method for controlling the expression of granulocyte/macrophage colony stimulating factor (GM-CSF) in cells which express GM-CSF, or for controlling the expression of other haemopoietic cytokines which contain the Ck-1 or Ck-2 DNA sequences in cells where they are expressed, which comprises the step of regulation of the binding of nuclear protein(s) in said cells with Ck-1 and Ck-2 in the promoter region of the GM-CSF gene or the said haemopoietic cytokine genes. The step of regulation of the binding of the nuclear protein(s) with Ck-1 and Ck-2 sequences may consist of the induction or promotion of binding, or alternatively, it may consist of the prevention or inhibition of binding. By way of example, regulation of the binding of the nuclear protein(s) may be effected by the use of DNA of a sequence which will act as a competitive inhibitor in the binding of protein(s).

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria
AU	Australia
BB	Barbados
BE	Belgium
BG	Bulgaria
BJ	Benin
BR	Brazil
CF	Central African Republic
CG	Congo
CH	Switzerland
CM	Cameroon
DE	Germany, Federal Republic of
DK	Denmark
FI	Finland
FR	France
GA	Gabon
GB	United Kingdom
HU	Hungary
IT	Italy
JP	Japan
KP	Democratic People's Republic of Korea
KR	Republic of Korea
LI	Liechtenstein
LK	Sri Lanka
LU	Luxembourg
MC	Monaco
MG	Madagascar
ML	Mali
MR	Mauritania
MW	Malawi
NL	Netherlands
NO	Norway
RO	Romania
SD	Sudan
SE	Sweden
SN	Senegal
SU	Soviet Union
TD	Chad
TG	Togo
US	United States of America

AMENDED CLAIMS

[received by the International Bureau on 13 March 1989 (13.03.89), original claim 1 amended; remaining claims unchanged (2 pages)]

1.(Amended) A method for controlling the expression of granulocyte/macrophage colony stimulating factor (GM-CSF) in cells which express GM-CSF, or for controlling the expression of other haemopoietic cytokines containing CK-1 or CK-2 in cells where they are expressed, which comprises the step of regulation of the binding of nuclear protein(s) in said cells with the promoter region of the GM-CSF gene or said haemopoietic cytokine genes.

2. A method according to claim 1, wherein said regulation step comprises induction or promotion of said binding of nuclear protein(s) with said promoter region.

3. A method according to claim 1, wherein said regulation step comprises prevention or inhibition of said binding of nuclear protein(s) with said promoter region.

4. A method according to claim 1, wherein said regulation step comprises regulation of binding of said nuclear protein(s) to the region spanning the cytokine-1 (CK-1) and/or cytokine-2 (CK-2) specific sequences of the promoter region of the GM-CSF gene.

5. A method according to claim 4, wherein said regulation step comprises induction of the formulation of the NF-GMa and/or NF-GMb complexes by interaction of nuclear protein(s) with said region spanning the CK-1 and/or CK-2 specific sequences.

6. A method of diagnosis of diseases associated with abnormalities in the expression of GM-CSF, which comprises the step of detection of abberations or abnormalities in

the identities of nuclear protein(s) in GM-CSF expressing cells, in the promoter region of the GM-CSF gene in said cells, or in the nature of binding of said nuclear protein(s) with said promoter region.

7. A method of diagnosis of diseases associated with the expression of GM-CSF which comprises the step of detection of the NF-GMa and/or NF-GMb nuclear protein(s) in cell samples taken from a patient.

8. A method for the determination of an agent which is effective in controlling the binding of nuclear protein(s) with the promoter region of GM-CSF gene in cells which express GM-CSF, which comprises the step of screening the effect of a candidate agent on a nuclear extract in a gel retardation assay.